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USAMRMC ltr, dtd 15 May 2003

AD_____

Award Number: DAMD17-98-1-8562

TITLE: Targeting Prostate Vasculture

PRINCIPAL INVESTIGATOR: Erkki Ruoslahti, M.D., Ph.D.

CONTRACTING ORGANIZATION: The Burnham Institute
La Jolla, California 92307

REPORT DATE: September 1999

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

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REPORT DOCUMENTATION PAGE

OMB No. 074-0188

1. AGENCY USE ONLY (Leave blank)	2. REPORT DATE	3. REPORT TYPE AND DATES COVERED
	September 1999	Annual (01 Sep 98 - 31 Aug 99)

4. TITLE AND SUBTITLE
Targeting Prostate Vasculture

5. FUNDING NUMBERS
DAMD17-98-1-8562

6. AUTHOR(S)
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8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSORING / MONITORING AGENCY REPORT NUMBER

11. SUPPLEMENTARY NOTES

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13. ABSTRACT ***(Maximum 200 Words)***

In this application, we propose to identify peptides that home to the vasculature of prostate. Peptides capable of homing to the prostate vasculature may allow imaging of the prostate for diagnostic purposes. They will also make it possible to direct into the prostate treatments that can reduce the size of the prostate and, therefore, reduce the risk of developing prostate cancer. During the first year of this grant, we have identified a peptide that homes specifically to mouse prostate tissue. We've determined, using the phage and peptide-biotin conjugates, that this peptide accumulates specifically in the prostate tissue after intravenous injection. Preliminary results from a phage overlay assay on human prostate tissue suggest that this peptide will home to human prostate vasculature. These results represent significant progress toward our goal of prostate imaging and targeting of therapies into the prostate.

14. SUBJECT TERMS	15. NUMBER OF PAGES
Prostate	7
	16. PRICE CODE

17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
Unclassified	Unclassified	Unclassified	Limited

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9-28-99

PI - Signature Date

This report contains unpublished results.

DAMD17-98-1-8562
Targeting Prostate Vasculature
PI: Erkki I. Ruoslahti, M.D., Ph.D.

This report contains unpublished results.

1. INTRODUCTION

The overall goal of this project is to complete the identification of prostate-homing molecules, and characterize their specificity. We will also determine the ability of the peptides to serve as carriers of materials such as imaging agents, drugs and radioisotopes into the prostate. Success in this project may make it possible to image the prostate for diagnostic purposes.

It will also make it possible to target treatments into the prostate. We will use the targeting to develop an animal model for prostatectomy by selective toxin ablation of the gland. We hope that this model will serve as a starting point for the development of a non-surgical prostatectomy and that reducing the size of the prostate will reduce the risk of developing prostate cancer. These studies may also provide a model for similar approaches to the treatment of premalignant and malignant conditions in other tissues.

2. PROGRESS REPORT

Technical Objective 1. To use *in vivo* screening of phage-displayed peptide libraries for identifying peptides capable of homing to prostate vasculature.

Objective 1 has been completed. We now have an excellent prostate homing peptide that gives a 30-40 fold enrichment of phage homing to prostate vasculature relative to other tissues. Coinjecting the synthetic peptide inhibits the homing of the phage, confirming the specificity of the homing. The peptide is heptapeptide, with the sequence SMSIARL. Because it is short and linear, it is easy to synthesize and to make into the conjugates needed in objectives 2 and 3.

Technical Objective 2. To characterize the tissue and species specificities of the prostate-homing peptides identified under Objective 1.

We also have made progress with Objective 2. Phage homing studies show that the SMSIARL phage homes specifically only to the prostate. Immunostaining reveals phage in the prostate vasculature within minutes of the intravenous injection, but later on the phage is found within the glandular epithelium. This is an unusual characteristic of this particular phage; we have not found any of our other organ-homing phage to enter the targeted tissue in that manner. It is a potentially useful characteristic for the targeting of therapeutic and diagnostic materials into the prostate. We also have preliminary evidence, obtained by using a phage overlay assay with human prostate tissue section, that the SMSIARL phage binds to the vasculature in the human prostate.

This report contains unpublished results.

Technical Objective 3. To evaluate the prostate-homing peptides as carriers of materials such as radionuclides into the prostate.

Work on Objective 3 has been initiated. We have coupled the prostate-homing peptide to biotin, and have shown that the conjugate accumulates in the prostate after an intravenous injection. We are now ready to proceed to the analysis of radionuclide targeting in a similar way.

3. KEY RESEARCH ACCOMPLISHMENTS

- Identified a heptapeptide, SMSIARL, that homes to specifically (and only) to prostate vasculature in mice
- Shown that biotinylated SMSIARL injected intravenously accumulates in prostate
- Preliminary results from overlay on human prostate tissue shows that SMSIARL may bind to human prostate vasculature

4. REPORTABLE OUTCOME

The results described above have been reported at meetings, and the first paper is in preparation.

5. CONCLUSIONS

We have an effective prostate-homing peptide. It is specific for the prostate vasculature, and it can direct a chemical (biotin) conjugated to it to accumulate in the prostate.

6. REFERENCES - none

7. APPENDIX - none

DEPARTMENT OF THE ARMY
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REPLY TO
ATTENTION OF

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